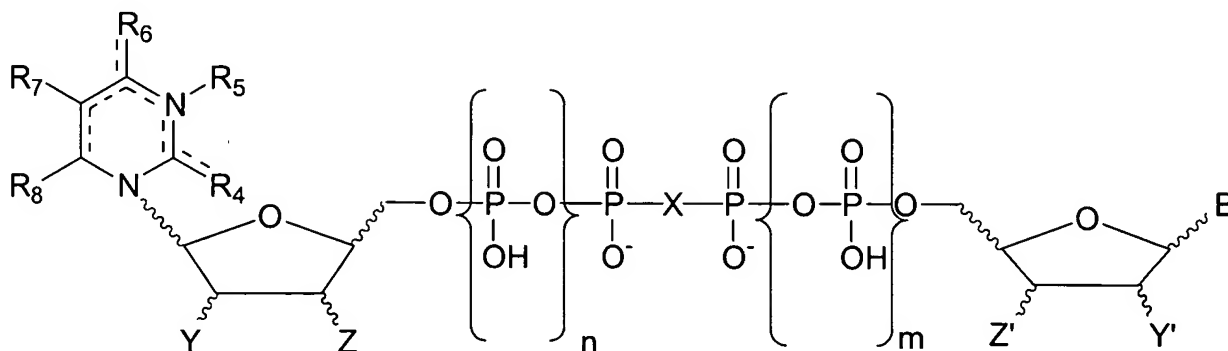


THE AMENDMENT

In the Claims

1. (Currently Amended) A compound of Formula IIIA:

Formula IIIA



wherein:

X is oxygen, methylene, difluoromethylene, imido;

n = 0, 1, or 2;

m = 0, 1, or 2;

n + m = 0, 1, 2, 3, or 4;

B is a purine or a pyrimidine residue linked through the 9- or 1-position, respectively;

Z = OH or N₃;

Z' = OH or N₃;

Y = H or OH;

Y' = H or OH;

provided that when Z is N₃, Y is H or when Z' is N₃, Y' is H;

R₄ is oxo, hydroxy, amino, cyano, aralkoxy, C₁₋₆ alkoxy, C₁₋₆ alkylamino, or dialkylamino;

R₅ is hydrogen, acyl, C₁₋₆ alkyl, phenyloxy, C₁₋₅ alkanoyl or

absent;

R₆ is oxo, hydroxy, mercapto, C₁₋₄alkoxy, C₇₋₁₂arylalkoxy, C₁₋₆alkylthio, amino, C₁₋₅ disubstituted amino, triazolyl, C₁₋₆alkylamino or di-C₁₋₄alkylamino, where the alkyl groups is optionally linked to form a heterocycle or link to N³ to form a substituted ring; or

R₅ and R₆ taken together form a 5-membered fused imidazole ring between positions 3 and 4 of the pyrimidine ring, which is optionally substituted on the 4- or 5- positions of the etheno moiety with C₁₋₄alkyl, phenyl, or phenyloxy, which themselves are optionally substituted;

R₇ is hydrogen, hydroxy, cyano, nitro, substituted and unsubstituted C₂₋₈alkenyl, phenyl, substituted and unsubstituted C₂₋₈alkynyl, halogen, CF₃, substituted and unsubstituted C₁₋₆alkyl, allylamino, bromovinyl, ethyl propenoate, propenoic acid; or

R₆ and R₇ taken together form a 5 or 6-membered saturated or unsaturated ring bonded through N or O at R₆, such ring optionally contain substituents that themselves contain functionalities;

R₈ is hydrogen, amino or di-C₁₋₄alkylamino, C₁₋₄alkoxy, C₇₋₁₂arylalkoxy, C₁₋₄alkylthio, C₇₋₁₂arylalkylthio, carboxamidomethyl, carboxymethyl, methoxy, methylthio, phenoxy or phenylthio; provided that when R₈ is amino or substituted amino, R₇ is hydrogen;

provided that when B = adenine, adenine 1-oxide, or 1,N⁶-ethenoadenine, then:

- (a) R₆ ≠ oxo when R₄ = oxo, Y = Z = OH and R₅ = R₇ = R₈ = H;
- (b) R₇ ≠ Br when R₄ = R₆ = oxo, Y = Z = OH, and R₅ = R₈ = H;

provided that when B = adenine, then:

- (a) R₆ ≠ amino when R₄ = oxo, Y = Z = OH, R₅ is absent, R₇ = R₈ = H, and
n + m = 0, 1, or 2;
- (b) R₇ ≠ CH₃ when R₄ = R₆ = oxo, Y = H, Z = OH, and R₅ = R₈ = H;
- (c) R₇ ≠ F when R₄ = R₆ = oxo, Y = H, Z = OH, R₅ = R₈ = H and n + m = 2;

provided that when B = thymine, Y' = H and Z' = N₃; then R₇ ≠ F, when R₄ = R₆ = oxo, Y = OH, Z = OH, R₅ = R₈ = H, and n + m = 0;

provided that when B = thymine, $Y' = H$ and $Z' = N_3$; then $R_7 \neq CH_3$ when $R_4 = R_6 =$
oxo, $Y = H$, $Z = N_3$, $R_5 = R_8 = H$, and $n + m = 0$;

provided that when B = guanine, then:

- (a) $R_6 \neq$ oxo when $R_4 =$ oxo, $Y = Z = OH$, $R_5 = R_7 = R_8 = H$ and $n + m = 1$ or 2 ;
- (b) $R_6 \neq$ amino when $R_4 =$ oxo, $Y = Z = OH$, R_5 is absent, $R_7 = R_8 = H$, $n+m=1$ or 2 ;

provided that when B is uridine, or 5-Br-uridine, then

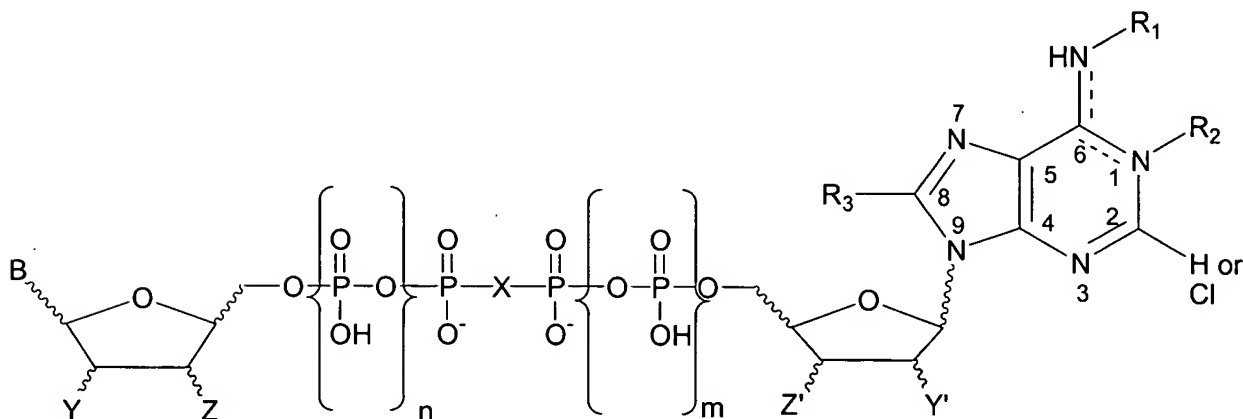
- (a) $R_6 \neq$ oxo when $R_4 =$ oxo, $Y = Z = OH$ and $R_6 = R_7 = R_8 = H$;
- (b) $R_7 \neq Br$ when $R_4 = R_6 =$ oxo, $Y = Z = OH$, and $R_5 = R_8 = H$;

provided that when B is 5-FU, then $R_7 \neq F$, when $R_4 = R_6 =$ oxo, $Y = H$, $Z = OH$, $R_5 = R_8$
 $= H$, and $n + m = 0$;

provided that when B is cytosine, then $R_6 \neq$ amino, when $R_4 =$ oxo, $Y = Z = OH$, R_5 is
absent, $R_7 = R_8 = H$, and $n + m = 1$, or 2 ; and

provided that when B is cytosine, then $R_6 \neq$ oxo, when $R_4 =$ oxo, $Y = Z = OH$ and $R_6 = R_5 =$
 $R_7 = R_8 = H$, and $n + m = 2$.

2. (Original) A compound according to Formula IIA:



FORMULA IIA

wherein:

X is oxygen, methylene, difluoromethylene, imido;

n = 0, 1, or 2;

m = 0, 1, or 2;

n + m = 0, 1, 2, 3, or 4;

B is a purine residue linked through the 9- position;

Z = OH or N₃;

Z' = OH or N₃;

Y = H or OH;

Y' = H or OH;

provided that when Z is N₃, Y is H or when Z' is N₃, Y' is H;

R₁ is H, C₁₋₈alkyl, phenyl or phenyloxy, optionally substituted with halogen, hydroxy, C₁₋₄alkoxy, C₁₋₄alkyl, C₆₋₁₀aryl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C₁₋₄ alkyl and when doubly substituted, the alkyl groups are optionally linked to

form a heterocycle; or $A(C_{1-6}\text{alkyl})\text{CONH}(C_{1-6}\text{alkyl})B$ wherein A and B are amino, mercapto, hydroxy or carboxyl;

R_2 is O or is absent; or

R_1 and R_2 taken together forms a 5-membered fused imidazole ring, which is optionally substituted on the 4- or 5- positions of the etheno moiety with C_{1-4} alkyl, phenyl or phenyloxy, optionally substituted with halogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{6-10} aryl, arylalkyl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C_{1-4} alkyl and when doubly substituted, the alkyl groups is optionally linked to form a heterocycle; and

R_3 is H, C_{1-8} alkyl, phenyl or phenyloxy, optionally substituted with halogen, hydroxy, C_{1-4} alkoxy, C_{1-4} alkyl, C_{6-10} aryl, carboxy, cyano, nitro, sulfonamido, sulfonate, phosphate, sulfonic acid, amino or substituted amino, wherein the amino is singly or doubly substituted by a C_{1-4} alkyl and when doubly substituted, the alkyl groups is optionally linked to form a heterocycle; C_{7-12} arylalkyl; C_{1-4} alkylamino, phenylamino, C_{7-12} arylalkylamino, C_{1-4} alkoxy, or C_{7-12} arylalkyloxy; C_{1-4} alkylthio, phenylthio, C_{7-12} arylalkylthio, or $-A(C_{1-6}\text{alkyl})\text{CONH}(C_{1-6}\text{alkyl})B-$ wherein A and B are independently amino, mercapto, hydroxy or carboxyl;

provided that $R_1 \neq H$, when X is oxygen, methylene, or difluoromethylene, Y is OH, B is adenine, R_2 is absent, and R_3 is hydrogen;

provided that $R_1 \neq H$, when $n + m = 2$, X is oxygen, Y is OH, B is adenine, R_2 is absent, and R_3 is bromo, or 6-aminoethyl;

provided that $R_1 \neq H$, when $n + m = 2$, X is oxygen, Y is H, B is adenine, R_2 is absent, and R_3 is H;

provided that $R_2 \neq O$, when $n + m = 2$, X is oxygen, Y is OH, $R_1 = R_3 = H$, and B is adenine, adenine 1-oxide, or 1, N^6 -ethenoadenine;

provided that R_1 and R_2 do not form a 5-membered fused imidazole ring, when $n + m = 2$, X is oxygen, Y is OH, R_3 is H, and B is adenine, adenine 1-oxide, or ethenoadenine.

3. (Original) The compound according to Claim 1 or 2, wherein the ribosyl moieties are in the D- configuration.

4. (Original) The compound according to Claim 1 or 2, wherein the ribosyl moieties are in the L- configuration.

5. (Previously Presented) A pharmaceutical composition comprising a compound of Formula IIIA or IIA as described in Claim 1 or 2, or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier therefor.

6. (Previously Presented) A method of treating chronic obstructive pulmonary diseases in a mammal by administering an effective chronic obstructive pulmonary disease treatment amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.

7. (Previously Presented) A method of treating sinusitis, otitis media or nasolacrimal duct obstruction in a mammal by administering an effective mucus secretion clearing amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.

8. (Previously Presented) A method of treating dry eye in a mammal by administering an effective dry eye treatment amount of a compound of Formula III A or IIA as described in Claim 1 or 2.

9. (Previously Presented) A method of treating retinal detachment in a mammal by administering an effective retinal detachment treatment amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2.

10. (Previously Presented) A method of facilitating sputum induction in a mammal by administering an effective amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2 to facilitate sputum induction.

11. (Previously Presented) A method of facilitating expectoration in a mammal by administering an effective amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2 to facilitating expectoration.

12. (Previously Presented) A method of treating cystic fibrosis in a mammal by administering an effective amount of a compound of Formula IIIA or IIA as described in Claim 1 or 2 to treat cystic fibrosis.

13. (Currently Amended) ~~The method according to Claim 12, wherein said compound is~~ A method of treating cystic fibrosis in a mammal by administering an effective amount of P¹-(2'-deoxycytidine 5'-)-P⁴-(uridine 5'-)tetraphosphate.